have been quinine and camphor and oil of cinnamon, and occasionally salicylates.

Relapses and repeated attacks have been very common in influenza, indicating causal organisms of unstable or less specific type, which do not readily call up in the tissues of the body an excess of response in the formation of natural antitoxins. I pointed out in 1906 [1] that symbiotic relationship of micro-organisms in the human body had yet to be studied in much more elaborate detail than in my own small contribution in that year. I believe that symbiosis has much to do with the evolution of pathogenic properties in organisms which are generally mere saprophytes. The relationship of bacteria to moulds is another department of bacteriological research which awaits organized study, and which will open up inexhaustible and fruitful mines of information to be applied in the treatment of infective diseases.[2]

Professor JOHN EYRE, M.D.

In March, 1917, I had the opportunity of investigating an outbreak in the Aldershot Command where the disease commencing with acute catarrhal symptoms, characteristic of "influenza," in a large percentage of the cases passed to a profound toxæmia with involvement of the bronchi and bronchioles and of the immediately adjacent pulmonary tissue in an interstitial—not lobar or lobular—pneumonia. This was labelled by those of us concerned in the inquiry as "purulent bronchitis." In these cases the expectoration throughout the whole course of the disease contained *Bacillus influenzæ*, at first the predominant, if not the sole, organism present, whilst lung punctures, too, yielded material which on culture gave a growth of *Bacillus influenzæ* either pure or associated with staphylococci, but no pneumococci. In the later stages the influenza bacillus was associated in the sputum with pneumococci, streptococci, *Micrococcus catarrhalis*, &c. The final stage of these cases was the entry of the pneumococcus into the blood stream and death from pneumococcic septicæmia. *Bacillus influenzæ* isolated from these cases possessed a high degree of virulence, and I was able to produce a fatal septicæmia, in four days, in the rabbit, after intrapulmonary inoculation. Previously I have never secured a fatal result with this organism in this animal save by intracranial inoculation.

[1] *Trans. Epid. Soc. Lond.*, 1905-6, n.s., xxv, pp. 204-244.

[2] *See* "Evolution and Disease," by J. T. C. Nash, M.D. (John Wright and Co., Bristol.)

In February, 1918, I again had the opportunity of inquiring into an outbreak in the Southern Command, where the history suggested that Colonial reinforcements had, on their way to England, acquired infection from America, where, as we now know from the evidence of Cole, McCallum and others, similar epidemic disease was prevalent, also associated with *Bacillus influenzæ* and, in addition, hæmolytic streptococci.

In this second investigation the early stages of the disease resembled those of the Aldershot epidemic, but in the progress of the disease broncho-pneumonia and even lobar pneumonia, often associated with pleuritic effusion (in which streptococci of the hæmolytic variety abounded) frequently occurred, and the termination was by streptococcic not pneumococcic septicæmia, but in all *Bacillus influenzæ* was the prominent organism in the early stages.

Subsequent outbreaks in different parts of England that I have had opportunities of observing have consistently exhibited the characteristics of the second type, that is to say, a primary *Bacillus influenzæ* infection, and in later stages the addition of streptococcic infection.

Since early last year, then, I have been closely in touch with the epidemic form of the disease in all parts of the country, and in my experience its early bacteriology has never varied. At the onset of the disease, when pyrexia and malaise are the outstanding features of the attack, nasal discharge and expectoration are usually absent or scanty, and pharyngeal mucus, nasal and post-nasal scrapings are alone available as material for examination. Later, tracheal mucus and nasal mucus may be obtained, although perhaps with some difficulty. Up to this point the microscopical appearances are always the same, viz., a groundwork of mucus, showing numerous leucocytes and thickly studded with minute Gram-negative bacilli, many exhibiting bipolar staining and thus simulating minute diplococci; frequently examples of both forms crowd the interior of the polynuclear cells. The cultures prepared from such material yield a good growth of *Bacillus influenzæ*, associated with occasional colonies of *Staphylococcus albus*, *Streptococcus brevis* and other similar saprophytes of the upper air passages. After an interval the mucus becomes distinctly purulent and coincidentally shows a much more varied flora—Gram-negative and Gram-positive diplo- and tetra-cocci in profusion, in addition to the Gram-negative bacillus, which is now much less easy to identify. Cultures at this stage show chiefly *Streptococcus longus*, usually *hæmolyticus* or *viridans*, or both, *Staphylococcus aureus*, *Micrococcus catarrhalis* and

pneumococcus; and *Bacillus influenzæ* is difficult, or almost impossible, to isolate except by the experimental inoculation of mice and rabbits.

In the severe and fatal cases all, or many, of the organisms already enumerated are present in the bronchial mucus and their presence may be shown by culture in the infected lung tissue. The organism most consistently present is *Bacillus influenzæ*, which is present also in the spleen pulp post mortem in association with the streptococcus or the pneumococcus which has caused the fatal septicæmia.

Personally I have not succeeded in isolating *Bacillus influenzæ* from the circulating blood during life, but I have had instances of its successful isolation brought to my notice by others.

My opinion, based upon the observations I have summarized, is that the epidemic is one of true influenza, due to *Bacillus influenzæ*, complicated in a large percentage of cases by secondary infections with pneumococcus or *Streptococcus longus*, var. *hæmolyticus*—one or other of these secondary infections being responsible for the terminal fatal septicæmia.

I consider that the *Bacillus influenzæ* completely fulfils the conditions required of an organism accused of specificity—that is to say, with the exception of the comparatively rare "carrier," it is absent from the upper air passages of the normal individual; it is capable of artificial cultivation and such artificial cultures are in turn capable of initiating the disease in man with recovery of the organism from the induced lesions.

The spraying of emulsions of *Bacillus influenzæ* into bottle cultures (for the preparation of massive growths for vaccine) has frequently provoked mild attacks of the clinical disease in those of us engaged in this work in my laboratory. (The production of specific antibodies in infected and vaccinated men and animals has also been observed, and I hope to make further reference to this point at some future date.)

In view of these results I fail to understand the attitude of those who, confronted with the available data, refuse to accept the obvious and seek some mysterious and elusive pathological virus, filter passer, or what not, to explain a pandemic which is the exact counterpart of the one which rather more than a quarter of a century ago prompted the investigations which led to the discovery of *Bacillus influenzæ;* and, on the other hand, readily accept the causative association of the pneumococcus or the streptococcus with the final and often fatal lesions.

Having thus clearly defined my conception of the bacteriology of the epidemic, obviously the next step was to inquire into the practicability

of prophylactic vaccination, not only against the prime cause of the disease but also against the associated bacteria responsible for the secondary infections. And here instant and sympathetic assistance was forthcoming from those in charge of the welfare of the N.Z.E.F., with the result that early in April, 1918, protective inoculations were instituted, and from the evidence at our disposal, seem to have been the means of conferring a considerable amount of immunity upon the New Zealanders in England through the primary wave of the pandemic in the summer months of this year. Our results were recorded by Captain Lowe and myself in the *Lancet* for October 12, 1918, p. 484, and need not be reiterated.

The serious incidence of the disease in a transport of colonial reinforcements which arrived in England at the end of September led to an even more extensive utilization of the prophylactic vaccine, but there has not yet been time to collect and collate the resulting figures.

I do not propose to discuss at length the dosage of the various components of the protective vaccine, since this is a matter depending almost entirely upon the methods of isolation, selection of strains and "distance of generation" from the human body.

This last factor is, in my opinion, of the highest importance, since by every subculture (or generation) a pathogenic organism is removed further from its original habitat in the pathological exudate, and this means a variable but distinct loss of virulence. I consider that if one obtains a pure growth of *Bacillus influenzæ* in a tube or plate planted directly from, we will say, tracheal mucus, a dose of 5 millions of the bacilli from that culture is equivalent in "antigen" content to a dose of 50 millions of the bacilli in the tube representing the fifth consecutive subculture from that original culture. And whilst I am aware that the 50 millions of bacilli from my fifth generation will provoke little, if any, more local and constitutional "reaction" than the 5 millions of bacilli from my original culture, I am not prepared to admit that the former will provoke as big an antibody response as the latter.

Whilst on this point I would further remark that the enormous doses suggested in connexion with commercial vaccines represent to my mind the large number of generations or subcultures that have intervened between the specimen from which the organism was isolated and the particular culture from which the vaccine was prepared—and coincidently the loss of virulence the organism has sustained.

Again, at the moment we have no accurate data as to the amount of

antigen that is utilized and the amount that is superfluous, and therefore wasted in any given dose of vaccine. Even the small doses I have advocated are ample to provoke a very smart local and constitutional reaction in weakly, though otherwise normal, individuals such as myself.

Major A. ABRAHAMS, R.A.M.C.

My remarks relate to some clinical features of the cases which we have been able to study in the Aldershot Command.[1] The Connaught Hospital, Aldershot, is devoted to the treatment of medical cases supplied by a very large number of troops in a highly concentrated area, and with a normal complement of 500 beds. We extended these to 850 to accommodate the large number of admissions during the recent epidemic.

I wish first to refer briefly to the condition known as "purulent bronchitis" in the light of the disease now under consideration: those of us who worked in Aldershot during the winters of 1915 and 1916 were struck by the existence of a peculiar type of lung affection with which we were hitherto unfamiliar. The patients manifested the signs more or less of bronchitis, broncho-pneumonia or lobar pneumonia; but the very special features were the expectoration of enormous quantities of purulent sputum, a most characteristic heliotrope-coloured cyanosis, and a very dreadful mortality.

It was not until Lieutenant-Colonel French was appointed consulting physician to the Aldershot Command that we began to see the proper significance of these cases. Hitherto I had been disposed to regard them as occurring for the most part in young men of feeble physique and of short service who were unable to endure the exposure entailed by ordinary military service; and the circumstance that the bulk of the cases occurred in one unit was speciously explained by the fact that this particular unit was at that time being largely recruited from men of low grade. Colonel French, however, objected very properly that such cases were by no means restricted to the type which supplied the majority, and further, that older men with good histories and comparatively long service were occasionally affected, and post-mortem examination supplied the puzzling evidence that the lungs were relatively free from disease. His alternative suspicion of some infective factor satisfactorily explained

[1] My colleague, Captain Hallows (p. 41), has already dealt with pathological details.